Express Mail No. EV328184656US
Date of Deposit: July 1, 2003

Attorney Docket No.: 23254-501

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS:	Holgersson *et al.*		
SERIAL NUMBER:	09/194,396	EXAMINER:	Gerald R. Ewoldt, Ph.D.
FILING DATE:	December 8, 1998	ART UNIT:	1644
FOR:	ANTIGENIC FUSION PROTEIN CARRYING GAL α1,3 GAL EPITOPES		

Director of the U.S. Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

July 1, 2003
Boston, Massachusetts

PETITION UNDER 37 C.F.R. § 1.181 FOR WITHDRAWAL OF HOLDING OF ABANDONMENT

1. Applicants request that the abandonment set forth in the Notice of Abandonment, mailed by the U.S. Patent and Trademark Office on June 25, 2003, be withdrawn.

2. Applicants submit that the Notice of Abandonment for failure to timely file a proper reply to the Office Letter mailed November 12, 2002 was sent in error. Applicants sent a response to the November 12, 2002 Office Action via facsimile on April 11, 2003. Because the time for response had not expired, Applicants filed a timely response.

3. Submitted herewith is:

   3.1 a copy of November 12, 2002 Office Action (5 pgs.) in the above identified application (Tab A);

   3.2 a copy of the Fax Cover Sheet (1 pg.), Amendment and Response to November 12, 2002 Final Office Action (8 pgs.) and courtesy copy of Hasemann and Capra, Fundamental Immunology, 2nd Edition (27 pgs.) filed via facsimile by Applicants' representatives on April 11, 2003 in the above identified application (Tab B);

   3.3 a copy of the Petition for Extension of Time (1 pg.) filed via facsimile by Applicants' representatives on April 11, 2003 in the above identified application (Tab C);

3.4 a copy of the Notice of Appeal (1 pg.) filed via facsimile by Applicants' representatives on April 11, 2003 in the above identified application (Tab D);

3.5 a copy of the June 25, 2003 Notice of Abandonment stating that Applicants failed to timely file a proper reply to the Office Letter mailed November 12, 2002 (2 pgs.) (Tab E);

3.6 a copy of the Certificate of Transmission under 37 C.F.R. 1.8 (1 pg.) filed via facsimile by Applicants' representatives on April 11, 2003 in the above identified application (Tab F);

3.7 a copy of the Fax Cover Sheet (1 pg.) sent via facsimile by Applicant's representatives on April 11, 2003, including a Transmission Report ("TX Report") indicating successful transmission of the items listed in Tab B (Tab G); and

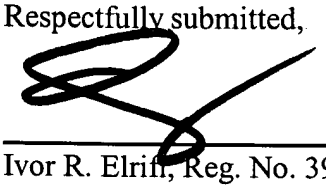
3.8 a copy of the Auto-Reply Facsimile Transmission from the United States Patent and Trademark Office, indicating receipt of 39 pages from Fax Sender at 617 542 2241 on April 11, 2003 at 2:41:16 pm (Tab H).

4. Accordingly, Applicants respectfully submit that the June 25, 2003 Notice of Abandonment was sent in error, and request that the abandonment be withdrawn.

5. No fee for this request is believed to be due. Should any additional fee be due, the Commissioner is hereby authorized to charge same, or credit any overpayment, to Deposit Account No. 50-0311 (Reference 23254-501). A duplicate copy of this request is enclosed.

6. Applicants request that acknowledgment be made of the active status of this application. The Examiner is invited to contact the undersigned with any questions at the telephone number listed below.

Respectfully submitted,



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07-02-03 1644

Express Mail Label No.: EV[redacted]184656US
Date of Deposit: July 1, 2003

Attorney Docket No. 23254-501

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Director of the U.S. Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

July 1, 2003
Boston, Massachusetts

TRANSMITTAL LETTER

Transmitted herewith for filing in the above-referenced patent application are the following documents:

1. Petition Under 37 C.F.R. §1.181 for Withdrawal of Holding of Abandonment (3 pgs); with Tabs A-H:
   - A. copy of November 12, 2002 Office Action in the above identified application (5 pgs.);
   - B. copy of the Fax Cover Sheet (1 pg.), Amendment and Response to November 12, 2002 Final Office Action (8 pgs.) and courtesy copy of Hasemann and Capra, Fundamental Immunology, 2nd Edition (27 pgs.) filed via facsimile by Applicants' representatives on April 11, 2003 in the above identified application (36 pgs. total);
   - C. copy of the Petition for Extension of Time filed via facsimile by Applicants' representatives on April 11, 2003 in the above identified application (1 pg.);
   - D. copy of the Notice of Appeal filed via facsimile by Applicants' representatives on April 11, 2003 in the above-identified application (1 pg.);
   - E. copy of the June 25, 2003 Notice of Abandonment stating that Applicants failed to timely file a proper reply to the Office Letter mailed November 12, 2002 (2 pgs.);

F. copy of the Certificate of Transmission under 37 C.F.R. 1.8 filed via facsimile by Applicants' representatives on April 11, 2003 in the above-identified application (1 pg.);

G. copy of the Fax Cover Sheet sent via facsimile by Applicant's representatives on April 11, 2003, including a Transmission Report ("TX Report") indicating successful transmission the items listed in Tab B (1 pg.); and

H. copy of the Auto-Reply Facsimile Transmission from the United States Patent and Trademark Office, indicating receipt of 39 pages from Fax Sender at 617 542 2241 on April 11, 2003 at 2:41:16 pm (1 pg.).

2. Return postcard.

If the enclosed papers are considered incomplete, the Mail Room and/or the Application Branch is respectfully requested to contact the undersigned at 617-542-6000, Boston, Massachusetts. A duplicate copy of this transmittal letter is enclosed.

The Commissioner is authorized to charge any additional fees that may be due, or to credit any overpayment, to the undersigned's account, Deposit Account No. 50-0311, Ref. No. 23254--501.

Respectfully submitted,

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TRA 1810188v1

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PATENT TRADEMARK OFFICE

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/194,396	12/08/1998	JAN HOLGERSSON	45115-53906	3163

30623 7590 11/12/2002

MINTZ, LEVIN, COHN, FERRIS, GLOVSKY AND POPEO, P.C.
ONE FINANCIAL CENTER
BOSTON, MA 02111

EXAMINER	
EWOLDT, GERALD R	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 11/12/2002

25

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/194,396	Holgersson et al.
Examiner	**Art Unit**
G.R. Ewoldt	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Aug 26, 2002*

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *15-19, 21-23, 25, 26, and 28-38* is/are pending in the application.

4a) Of the above, claim(s) *15-19* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *21-23, 25, 26, and 28-38* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. During a telephone conversation with Ivor Elrifi on 9/17/01, Applicant indicated that should a restriction election be required, Applicant would elect the Group comprising the fusion protein product. Affirmation of this election was requested in the last action, mailed 11/20/01. Applicant has failed to address the request. Affirmation of this election must be made by Applicant in replying to this Office action. Applicant is advised that failure to again confirm the election in response to this action will be considered non-responsive.

2. Claims 21-23, 25-26, and 28-38 are being acted upon.

3. In view of Applicant's amendment and response, filed 8/26/02, only the following rejections remain.

4. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 25-26 and 28 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed, for the reasons of record as set forth in Paper No. 18, mailed 11/20/01. This is a new matter rejection.

Applicant's arguments, filed 8/26/02, have been fully considered but they are not persuasive. Applicant argues that Claim 25 has been canceled, however, the claim is still pending. Applicant argues that the experiment disclosed on page 12 of the specification supports the claim to the fusion protein of Claim 21, wherein the first polypeptide comprises more Galα1,3Gal epitopes than a wild-type P-selectin glycoprotein ligand-1. Said single experiment discloses a single construct that may have the claimed property, however, the claim recites a generic "first polypeptide" that cannot be supported by the single species disclosed in the example. Note that a genus may not support a subgenus even though there is a disclosed species within the genus and a subgenus is not necessarily described by a genus

encompassing it and a species upon which it reads, *In re Smith* 173 USPQ 679, 683 (CCPA 1972). See MPEP 2163.05(b).

6. The following are New Grounds for Rejection necessitated by Applicant's amendment.

7. Claims 21-23, 25-26, and 28-38 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) "the second polypeptide comprises an immunoglobulin heavy chain polypeptide." (Claim 21, 25, 26, and 29),

B) "wherein the first polypeptide comprises the extracellular portion of a P-selectin glycoprotein ligand-1 ..." (Claim 29),

C) "wherein the first polypeptide comprises more Galα1,3Gal epitopes than a wild-type P-selectin glycoprotein ligand-1." (Claim 33 and 38)

D) "wherein the first polypeptide comprises a part of a P-selectin glycoprotein ligand-1 that mediates binding to selectin ... (Claim 34).

Applicant argues that support for a fusion protein comprising a heavy chain immunoglobulin can be found in the specification at page 5 in the recitation of "an immunoglobulin or [a] part thereof." Applicant is advised that a generic disclosure, i.e., a part of an immunoglobulin, is insufficient support for the recitation of a specific part, i.e., a heavy chain, see paragraph 5 above. Likewise, the single disclosure of the experiment on page 12 of the specification cannot support the generic recitations Claims 29, 33, and 38. Note that the recitation of a wild-type P-selectin glycoprotein ligand-1 in Claims 33 and 38 indicates that the claim is intended to be generic, i.e., more that one wild-type P-selectin glycoprotein ligand-1 exist. Regarding Claim 34, no support for the limitations of the claim have been indicated and none have been found in the specification.

8. No claim is allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Patrick J Nolan

G.R. Ewoldt, Ph.D.
Patent Examiner
Technology Center 1600
November 8, 2002

Patrick J. Nolan, Ph.D.
Primary Examiner
Technology Center 1600

MINTZ LEVIN COHN FERRIS GLOVSKY AND POPEO PC

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Fax Cover Sheet

DATE: April 11, 2003

FROM: Cynthia A. Kozakiewicz, Ph.D.

Direct Dial 617 348 4452
ckozakiewicz@mintz.com

TO:

NAME	COMPANY	BUSINESS #	FAX #
Examiner Gerald Ewoldt	US Patent and Trademark Office		703 872-9305

MESSAGE:

Re: U.S.S.N. 09/194,396
Title: ANTIGENIC FUSIONPROTEIN CARRYING GALa 1,3 GAL EPITOPES
Filed: December 8, 1998
Attorney Docket No. 23254-501

We are sending a total of 37 pages, including this cover sheet.

Please call us at 617.348.4966, if you experience any problems.

By Facsimile: 703 872 9305
Date of Transmission: April 11, 2003

Attorney Docket No.23254-501

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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SERIAL NUMBER :	09/194,396	EXAMINER :	G. Ewoldt
FILING DATE :	December 8, 1998	ART UNIT :	1644
FOR :	ANTIGENIC FUSIONPROTEIN CARRYING GALα 1,3GAL EPITOPES		

BOX AF
Assistant Commissioner for Patents
Washington, D.C. 20231

AMENDMENT AND RESPONSE TO NOVEMBER 12, 2002 FINAL OFFICE ACTION

This paper is in response to the November 12, 2002 Final Office action. A petition for a two-month extension of time is filed herewith. With this extension of time, this response is due on or before April 14, 2003 (April 12, 2003 being a Saturday). No other fee is believed due in connection with this response. The Commissioner is hereby authorized to charge the fee for the two-month extension of time and any additional fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. 23254-501 (AB-1).

In the claims:

Please cancel claims 15-19 without prejudice or disclaimer as directed to non-elected inventions. Cancel claim 25, amend claims 28, 33 and 38 and replace the pending claims with the following:

21. A dimerized fusion polypeptide comprising a first polypeptide operably linked to a second polypeptide, wherein the first polypeptide:

(a) comprises a P-selectin glycoprotein ligand-1; and

(b) is glycosylated by an α1,3 galactosyltransferase and

the second polypeptide comprises an immunoglobulin heavy chain polypeptide.

22. The fusion polypeptide of claim 21, wherein the first polypeptide comprises multiple Galα1, 3Gal epitopes.

23. The fusion polypeptide of claim 21, wherein the α1,3 galactosyltransferase is porcine.

26. The fusion polypeptide of claim 21, wherein said second polypeptide comprises an Fc region of an immunoglobulin heavy chain.

28. (Amended) The fusion protein of claim 21, wherein the first polypeptide comprises more Galα1, 3Gal epitopes than the human wild-type P-selectin glycoprotein ligand-1 polypeptide.

29. A dimerized fusion polypeptide comprising a first polypeptide operably linked to a second polypeptide, wherein the first polypeptide:

(a) comprises the extracellular portion of a P-selectin glycoprotein ligand-1; and

(b) is glycosylated by an α1,3 galactosyltransferase and

the second polypeptide comprises immunoglobulin heavy chain polypeptide.

30. The fusion polypeptide of claim 29, wherein the first polypeptide comprises multiple Galα1, 3Gal epitopes.

31. The fusion polypeptide of claim 29, wherein the α1,3 galactosyltransferase is porcine.

32. The fusion polypeptide of claim 29, wherein said second polypeptide comprises an Fc region of an immunoglobulin heavy chain.

33. (Amended) The fusion protein of claim 29, wherein the first polypeptide comprises more Galα1, 3Gal epitopes than the human wild-type P-selectin glycoprotein ligand-1 polypeptide.

34. A dimerized fusion polypeptide comprising a first polypeptide operably linked to a second polypeptide, wherein the first polypeptide:

(a) comprises a part of a P-selectin glycoprotein ligand-1 that mediates binding to selectin; and

(b) is glycosylated by an α1,3 galactosyltransferase and

the second polypeptide comprises an immunoglobulin polypeptide.

35. The fusion polypeptide of claim 34, wherein the first polypeptide comprises multiple Galα1, 3Gal epitopes.

36. The fusion polypeptide of claim 34, wherein the α1,3 galactosyltransferase is porcine.

37. The fusion polypeptide of claim 34, wherein said second polypeptide comprises an Fc region of an immunoglobulin heavy chain.

38. (Amended) The fusion protein of claim 34, wherein the first polypeptide comprises more Galα1, 3Gal epitopes than the human wild-type P-selectin glycoprotein ligand-1 polypeptide.

REMARKS

Upon entry of the foregoing amendments, claims 21-23, 26, and 28-38 are under consideration. Claims 15-19 were canceled without prejudice or disclaimer as directed to non-elected inventions. Support for the amendment to claims 28, 33 and 33 is found in the specification at page 8, lines 3-6. No new matter is added.

Restriction Requirement

In response to the Restriction Requirement dated November 20, 2001, Applicants elect the invention of Group I (claims 21-26 and 28), drawn to a dimerized fusion protein, without traverse.

§ 112, First Paragraph Rejection: Written Description

1. The Examiner has rejected claims 25-26, and 28 under 35 USC § 112 first paragraph for lack of written description. The Examiner asserts that the specification and the claims as originally filed does not provide support for the invention as now claimed. The Examiner states that claim 25 is still pending. In response, Applicants note that claim 25 has been canceled herein. Therefore, this rejection is moot as it pertains to claim 25. The remaining rejections are addressed as follows.

1A. "more Galα1, 3Gal epitopes than a wild-type P-selectin glycoprotein ligand-1"

The Examiner states that "Applicant argues that the experiment disclosed on page 12 of the specification supports the claim to the fusion protein of claim 21, wherein the first polypeptide comprises more Galα1, 3Gal epitopes than a wild-type P-selectin glycoprotein ligand-1." (See Final Office Action, page 2). In response, Applicants assert that pending claim 21 does not recite the phrase "more Galα1, 3Gal epitopes than a wild-type P-selectin glycoprotein ligand-1." Applicants would like to note to the Examiner that claim 26, which depends from claim 21, does not recite this phrase. Applicants further note that claim 28, which depends from claim 21, as ameded herein recites in part, "wherein the first polypeptide comprises more Galα1, 3Gal epitopes than the human wild-type P-selectin glycoprotein ligand-1 polypeptide." Applicants address this rejection as it applies to claim 28. The specification

discloses at, *e.g.*, page 11, lines 12-37 and Figure 1, that fusion proteins containing the human PSGL-1 polypeptide that are glycosylated by an α1,3 galactosyltransferase contain more Galα1, 3Gal epitopes than the human wild-type P-selectin glycoprotein ligand-1 polypeptide, as shown by Western blotting with the *Bandereria simplicifolia* isolectin B_4 (See Figure 1, right column). Applicants have amended claim 28 herein to recite the phrase "wherein the first polypeptide comprises more Galα1, 3Gal epitopes than the human wild-type P-selectin glycoprotein ligand-1 polypeptide." Applicants assert that the recitation of the phrase "the human wild-type P-selectin glycoprotein ligand-1 polypeptide" is a single species, and thus, that one skilled in the art could readily determine if the claimed polypeptide falls within its scope. Thus, claim 28 as amended herein is fully supported by the as filed specification. Therefore, this rejection should be withdrawn.

2. The Examiner has rejected claims 21-23, 25-26, and 28-38 under 35 USC § 112 first paragraph for lack of written description. The Examiner asserts that the specification and the claims as originally filed does not provide support for the invention as now claimed. Claim 25 has been canceled herein. Therefore, this rejection is moot as it pertains to claim 25. The remaining rejections are addressed as follows.

2A. "an immunoglobulin heavy chain polypeptide"

Regarding claims 21, 25, 26, and 29, the Examiner states that the specification and the claims as originally filed do not provide support for the phrase "an immunoglobulin heavy chain polypeptide." Applicants have canceled claim 25. Thus, this rejection is moot as it applies to this claim. Applicants traverse this assertion to the extent it applies to claims 21, 26 and 29. Applicants assert that the specification at page 8, lines 6-10, recites that "[t]he mucin/immunoglobulin expression plasmid was constructed by fusing the PCT-amplified cDNA of the extracelluar part of PSGL-1 in frame via a BamHI site, to the Fc part (hinge, CH2 and CH3) of mouse IgG_{2b} carried as an expression casette in CDM7." It is known to one of ordinary skill in the art that the Fc (fragment crystallizable) region of an IgG inherently contains an immunoglobulin heavy chain polypeptide, particularly since the immunoglobulin light chain polypeptide is not present in the Fc region, as it is contained within the F(ab) region of an IgG. (See, *e.g.*, Figure 1, Chapter 9, pages 209-233 of Fundamental Immunology, 2nd Edition, W.E. Paul, *ed.*, Raven Press, NY; courtesy copy enclosed).

A structure or process not explicitly described may meet the conveyance standard if it is "inherent" in what is described. See Standard Oil Co. v. Montedison, S.p.A., 494 F.Supp 370 (D. DE 1980) ("[p]atent entitlement is based on scientific skill and diligence and not on the ability to manipulate the English language, . . . Legal equivalence, or inherency, may be established either by the direct meaning of the language or by inferenced drawn from the terms of the initial disclosure." In the pending application, one skilled in the art would reasonably conclude that Applicant's disclosure of the Fc region of an IgG inherently discloses an immunoglobulin heavy chain polypeptide, and, therefore, that the Applicants had possession of the claimed invention at the time the application was filed. Thus, pending claims 21, 26, and 29 are fully supported by the as filed specification.

2B. "the extracellular portion of a P-selectin glyoprotein ligand-1"

Regarding claim 29, The Examiner states that the specification and the claims as originally filed do not provide support for the phrase "extracellular portion of a P-selectin glyoprotein ligand-1." Applicants traverse. The specification at page 8, lines 6-8, recites that "[t]he mucin/immunoglobulin expression plasmid was constructed by fusing the PCR-amplified cDNA of the extracelluar part of PSGL-1 in frame via a BamHI site." (Emphasis added). The plain meaning of the term "part" is "a division, portion or segment of a whole." (Webster's II New Riverside Dictionary, Revised, 1996). "Patent entitlement is based on scientific skill and diligence and not on the ability to manipulate English synonyms." Standard Oil Co. v. Montedison, S.p.A. 494 F. Supp. 370, 384 (D. Del. 1980). Therefore, the phrase "extracellular portion of a P-selectin glyoprotein ligand-1" as used in claim 29 is fully supported by the as filed specification.

2C. "more Galα1, 3Gal epitopes than a wild-type P-selectin glycoprotein ligand-1"

Regarding claims 33 and 38, The Examiner states that the specification and the claims as originally filed do not provide support for the phrase "comprises more Galα1, 3Gal epitopes than a wild-type P-selectin glycoprotein ligand-1." In response, Applicants note that claims 33 and 38 have been amended herein to recite "comprises more Galα1, 3Gal epitopes than the human wild-type P-selectin glycoprotein ligand-1 polypeptide." (Emphasis added). As noted above, the specification discloses at, *e.g.*, page 11, lines 12-37 and Figure 1, that fusion proteins containing the human PSGL-1 polypeptide that are glycosylated by an α1,3 galactosyltransferase

contain more Galα1, 3Gal epitopes than the human wild-type P-selectin glycoprotein ligand-1 polypeptide, as shown by Western blotting with the *Bandereria simplicifolia* isolectin B_4. Therefore, claims 33 and 38 as amended herein are fully supported by the as filed specification.

2D. "comprises a part of a P-selectin glycoprotein ligand-1 that mediates binding to selectin"

Regarding claim 34, The Examiner states that the specification and the claims as originally filed do not provide support for the phrase "comprises a part of a P-selectin glycoprotein ligand-1 that mediates binding to selectin." In response, Applicants assert that claim 34 is fully supported; the specification at page 4, lines 34-36, recites "in a preferred embodiment, the antigenic fusion protein according to the invention further comprises a part, which mediates binding to selectin, such as P-selectin." The specification further discloses at page 5, lines 6-9 that "the part that mediates binding to selectin is the P-selectin glycoprotein ligand-1 (PSGL-1) or an essential part thereof." Therefore, pending claim 34 is fully supported by the as filed specification. These rejections can be withdrawn.

CONCLUSION

Applicants believe that the claims, as amended, are in condition for allowance. If the Examiner has any questions, the Examiner is invited to contact the undersigned by telephone.

Respectfully submitted,

42,764

Dated: April 11, 2003

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Version Marked to Show Changes

Claims 28, 33 and 38 have been amended as follows:

28. (Amended) The fusion protein of claim 21, wherein the first polypeptide comprises more Galα1, 3Gal epitopes than the human [a] wild-type P-selectin glycoprotein ligand-1 polypeptide.

33. (Amended) The fusion protein of claim 29, wherein the first polypeptide comprises more Galα1, 3Gal epitopes than the human [a] wild-type P-selectin glycoprotein ligand-1 polypeptide.

38. (Amended) The fusion protein of claim 34, wherein the first polypeptide comprises more Galα1, 3Gal epitopes than the human [a] wild-type P-selectin glycoprotein ligand-1 polypeptide.

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9

Immunoglobulins: Structure and Function

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The relationship between the structure and function of the immunoglobulin molecule is a tribute to the power of molecular evolution. Via the duplication and diversification of the immunoglobulin homology domain, a family of molecules with diverse biological functions has been derived (1–3). The seemingly paradoxical relationship between uniformity and diversity is one of the things that makes the study of immunoglobulins interesting and rewarding.

Immunoglobulins are the prototype members of the immunoglobulin supergene family (4). This family of molecules shares a conserved protein sequence that represents the duplication of a primordial gene segment. As is made clear later, it is the linear combination of two or more of these segments that forms an immunoglobulin heavy or light chain. There are several other molecules that are also derived from this primordial sequence element, such as the CD4 and CD8 molecules (see Chapter 4), the antigen specific chains of the T cell receptor (see Chapter 11), and both the class I and class II MHC antigens (see Chapter 17) to name a few. Three-dimensional analyses of molecules that contain these immunoglobulin-like domains have revealed that there is more than simply an amino acid sequence homology between them; this conserved sequence represents a structural motif that can be used as a subunit in building large macromolecules (5,6). Thus there has been conservation of this immunoglobulin homology domain throughout evolution such that not only are immunoglobulin heavy and light chains strikingly similar to each other, but similar to a variety of other molecules as well.

As similar in structure as these molecules are, variation is the underlying essence of antibody function. Through the switch from one heavy chain isotype to another, the functional nature of the immune response can be altered significantly (see Chapter 14). Complement fixation, the ability to cross the placenta, and the ability to form multimers are just a few of the variations in antibody function due to isotypic differences (7–9). Each of these different biological responses is due to discreet differences in antibody structure.

The truly remarkable feature of antibody function, however, is the ability to recognize specific antigenic determinants. The potential repertoire of distinct antibody

specificities is, for all practical purposes, infinite. This function is attributed to the variable domains of the heavy and light polypeptide chains of any given antibody (10). While called the "variable" region, any two variable regions are likely to be from 70 to 99% identical, and even those that have only a single amino acid difference can demonstrate distinct antigenic specificities. Thus, through only slight variations in structure, the entire antibody repertoire of an individual is determined. The intent of this chapter is to emphasize the details of antibody structure which allow this simple class of molecules to function in such a variety of elegant ways.

IMMUNOGLOBULIN STRUCTURE

General Immunoglobulin Features

A prototypic immunoglobulin molecule is composed of four polypeptide chains which are joined into a macromolecular complex via several disulfide bonds (5). Figure 1 is a diagram of such a prototypic molecule. The smaller polypeptide is called a light chain and the larger a heavy chain. An antibody molecule is composed of two identical light chains and two identical heavy chains. The exclusive use of one heavy chain sequence and one light chain sequence is the consequence of allelic exclusion, a genetic event that is detailed in Chapter 10. The net result of allelic exclusion is that only one light chain gene and one heavy chain gene are expressed in any antibody-producing cell, and thus two identical heavy chain polypeptides and two identical light chain polypeptides are assembled into a single immunoglobulin molecule.

Based on experiments with proteolytic enzymes such as papain or trypsin, which cleave the immunoglobulin molecule at specific points, the molecule can be divided into two basic functional domains (10). As Fig. 1 shows, there are two F_{ab} fragments consisting of a light chain and a fragment of the heavy chain. The name F_{ab} is derived from the fact that this portion of the molecule contains the antigen-binding (ab) activity of the molecule. The remaining portion, the F_c fragment, is so named because it is easily crystallized (c). The F_c portion of the molecule is responsible for the biological effector functions of the immunoglobulin molecule, such as complement fixation. Another proteolytic fragment, $F(ab)'_2$ consists of the two F_{ab} fragments plus the portion of the heavy chain that contains one or more interchain disulfide bonds. Thus the $F(ab)'_2$ fragment is divalent, unlike the F_{ab} fragment which is univalent.

Early studies of immunoglobulin structure often used the immunoglobulin as an antigen (reviews in refs. 11 and 12). Human myeloma proteins, the antibody product of a plasma cell malignancy (and later, mouse plasmacytomas and hybridomas), were used as a homogeneous source of immunoglobulin for these studies. In this way heterologous antisera were created which, after several adsorption steps, would subdivide immunoglobulins into a finite number of groups. These groups, termed isotypes, are the serological consequence of the fact that there are

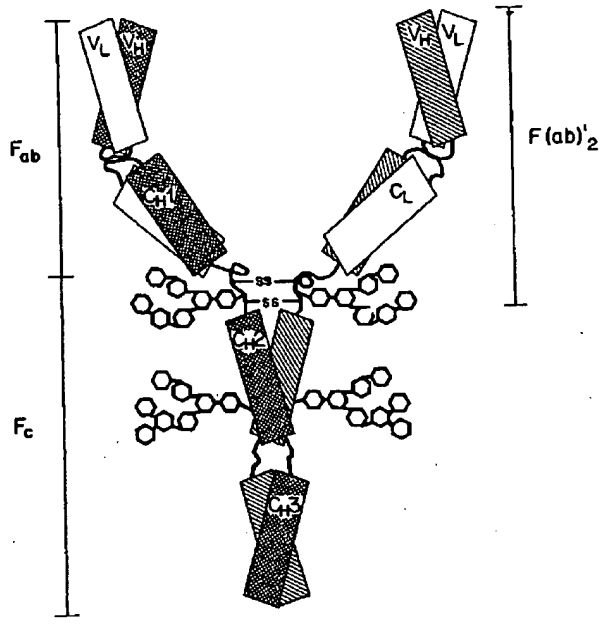

FIG. 1. Diagram of a prototypic immunoglobulin monomer. Each *rectangle* represents an immunoglobulin domain, with the extended polypeptide strands connecting the domains into complete heavy (*dark shading*) and light (*light shading*) chains. The interchain disulfide bonds between the hinge regions of the heavy chains are represented as *black bars*. Intrachain and interchain disulfides between heavy and light chains are not shown. Carbohydrate groups are shown connected to both the hinge regions and the second constant region domain of each heavy chain. The boundaries of the major proteolytic fragments are indicated by the *bars* to the left and right of the figure. Note that the F_{ab}/F_c division occurs above the interchain disulfides, while the $F(ab)'_2$ division is below.

several different kinds of heavy and light chain constant regions. There are five heavy chain classes, designated by the Greek letters mu (μ), delta (δ), gamma (γ), alpha (α), and epsilon (ϵ). There are two light chain types, kappa (κ) and lambda (λ). The isotype of a given antibody molecule depends on the class of heavy chain and the type of light chain that are used. A common notation to designate the isotype of an antibody is to follow the antibody name with the appropriate Greek letters, for example, MOPC104E ($\mu\lambda$). Since the effector functions of the antibody are a consequence of the heavy chain only, it is often sufficient to refer to the heavy chain class alone. Thus IgM refers to antibodies utilizing a μ chain, IgG for γ, and so on. The use of immunoglobulins as antigens, and the various antigenic markers that immunoglobulins bear, are discussed further in the final section of this chapter.

Each heavy and light chain can be divided into domains, each domain consisting of approximately 110 amino acids. The light chain consists of two domains, indicated as V_L and C_L (Fig. 1). V_L is the variable region of the light chain and is the region of the light chain which participates in

antigen binding. C_L is the constant region of the light chain, which is essentially invariant for a given light chain type. The heavy chain also has a variable region, V_H, which as in the light chain is the portion of the polypeptide that participates in antigen binding. In contrast to the light chain, the prototype heavy chain has three constant domains, C_H1, C_H2, and C_H3. In addition, the heavy chains of most immunoglobulins have a region known as the hinge (generally located between C_H1 and C_H2), which give the F_{ab} portions of the molecule considerable freedom to move about in relation to the F_c. In both heavy and light chains the variable and constant regions are encoded by separate genes (13). This means that any V_H or V_L region can be combined with any C_H or C_L region, respectively. Thus the ability to recognize a given antigen (a V region property) can be linked to any of the various effector functions (a C region property).

As indicated previously, each of these V and C domains bears a sequence homology that indicates that they were at one time derived from a common ancestral gene. One important feature of this domain structure is the presence of two cysteines which form an intramolecular disulfide bond. With rare exceptions, there is one disulfide bond per domain, and this is always an intradomain bond. This bond is thought to be important for maintaining the tertiary structure of the immunoglobulin subunit as described in a later section. Disulfide bonds are important to the quaternary structure of the immunoglobulin molecule as well (14). The light chain is generally attached to a heavy chain by a disulfide bond, and, in turn, the heavy chains are covalently linked to one another by disulfide bridges between the hinge units. This pattern of disulfide bonding results in a molecule that can be thought of as composed of two identical half molecules, each consisting of a single heavy and light chain pair. Each heavy and light chain pair has the capacity to recognize and bind the same epitope. Thus an intact immunoglobulin molecule can interact with two epitopes simultaneously. This characteristic of immunoglobulin structure gives an immunoglobulin monomer a binding valence of two. Experimental determinations of the actual valence of immunoglobulin monomers give a value slightly less than two. This difference is believed to be due to steric hindrance and other thermodynamic considerations.

Immunoglobulins also occur in multimers, which are covalently bound concatamers of the basic immunoglobulin monomer. Not all isotypes of immunoglobulin form multimers. Specifically, IgA usually forms a dimeric molecule, and IgM forms a pentameric molecule. Both of these macromolecules utilize an accessory molecule called J chain to form these complexes (reviewed in ref. 15). Immunoglobulin multimers have higher valences for antigen binding roughly proportional to the additional number of binding sites in the molecule. In addition, the secreted forms of IgA are associated with a molecule called secretory component (SC), which is involved in immunoglobulin transport across epithelial membranes (16).

Finally, immunoglobulins are glycoproteins and, with some exceptions, glycosylation is restricted to the constant region of the heavy chain. Different heavy chain classes have different types of carbohydrate groups and different locations of carbohydrate attachment. The prototypic molecule shown in Fig. 1 has carbohydrate attached both in the hinge region and in the second constant region domain. This carbohydrate is thought to be important for correct immunoglobulin folding and transport during synthesis (17) and appears to regulate the turnover rate of immunoglobulin. No effector functions have been directly attributed to carbohydrate. In the section on heavy chains to follow, variation in carbohydrate content is discussed more completely.

The Immunoglobulin Domain

As mentioned previously, immunoglobulins are composed of the linear combination of a basic subunit structure. This subunit, or domain, has a compact globular structure in three dimensions. Figure 2 is a schematic representation of data derived from X-ray diffraction studies of an immunoglobulin light chain (18). The solid arrows represent the seven polypeptide strands that comprise the antiparallel β-pleated sheets in an immunoglobulin domain. Each domain contains two such β-pleated sheets, one β sheet consisting of four β strands, the other consisting of three β strands. These β sheets form a "hydrophobic sandwich" between them. The numbering of the β strands reflects which layer the strand is in, either the four stranded sheet or the three. The two β sheets are covalently linked by a disulfide bond. The half cystines that form this bond are conserved in all molecules that possess immunoglobulin domains. The loops that connect the β strands are frequently glycine rich, which increases their flexibility. This structural motif, two β sheets forming a barrellike structure with a hydrophobic core, is referred to as the "immunoglobulin fold" or more generally a "β barrel." All the immunoglobulin constant region domains maintain this same basic structure. The variable region domains have a slightly different structure, wherein several of the loops connecting the β strands (those at the right end of Fig. 2) are somewhat longer.

The polypeptide strand connecting the V and C (C_L or C_H1) domains is called the switch. The switch is important to antibody structure because of the flexibility it allows between the V and C domains. One particularly important feature of this flexibility is that it allows the two domains to rotate relative to one another. Figure 2 demonstrates the importance of this rotation; note that the four-stranded β sheet of the C domain is on top, while in the V domain, the three-stranded sheet is on top. When a heavy chain and light chain combine to form an intact H–L pair as depicted in Colorplate 1 (see page 220), the C_H and C_L domains make close contacts between the two four-stranded sheets, while V_H and V_L pair via the three-stranded sheets (19). The C_H–C_L pairing creates a compact hydrophobic core between the β sheets forming an anchor for the V domains. The V_H–V_L pairing has a more hydrophilic groove formed by the three-stranded sheets forming a pocket in which small molecules can fit. This groove, together with the loops at the end of the V regions, form the antibody-combining site for antigen.

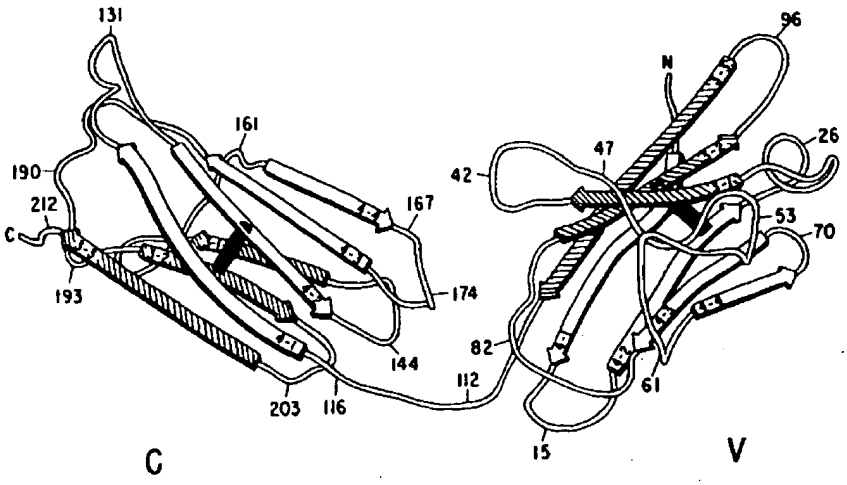

FIG. 2. Schematic drawing of the V and C domains of a light chain. The β strands participating in the antiparallel β-pleated sheets of each domain are represented as *arrows*. The β strands of the three-stranded sheets are *shaded*, while those in the four-stranded sheets are *white*. The β strands are numbered according to the scheme of Edmundson. The intradomain disulfide bonds are represented as *black bars*. Selectec amino acids are numbered, with position 1 as the N terminus. (From Edmundson et al., ref. 18, with permission.)

It is clear from this background of immunoglobulin structure that the three-dimensional structure of the immunoglobulin fold places a considerable constraint on the primary structure of immunoglobulin domains. The following sections examine the primary structures of heavy and light chains, and how several immunoglobulin domains combine to form distinct quaternary structures with distinct biological functions.

Heavy Chains

Heavy chains can be divided into three functional regions: F_d, hinge, and F_c. F_d in combination with a light chain forms F_{ab}, which has all the antigen-binding properties of an intact immunoglobulin. F_d can be subdivided further into the V_H and C_H1 domains, wherein V_H possesses all the antigen-binding properties and C_H1 acts mostly as an anchor (holding the variable region stable) and as a spacer (moving the antigen-binding portion of the molecule further from the F_c fragment). The hinge acts as a more flexible spacer, allowing the F_{ab} fragments to move more freely in space. Finally, the F_c fragment bears the effector functions of the immunoglobulin molecule. Each F_c fragment can occur in two forms, the membrane and secreted forms. The difference between these forms is found in the carboxy terminus, with the membrane form having a long hydrophobic stretch which anchors the polypeptide in the cell membrane. These alternate forms are achieved via alternative mRNA processing from the same primary transcript (see Chapter 10).

Constant Regions

The constant regions of the human heavy chains, including two subclasses of α (α_1, α_2), are diagrammed in Fig. 3. Subclasses represent a more recent duplication of a constant region gene. The α class has two subclasses in the human (α_1, α_2), but the distribution of subclasses varies in other species. The most apparent variations in heavy chain structure involve the hinge region and carbohydrate attachments, although more subtle structural differences can be found in the primary structures of C_H1 and F_c.

C_H1 and F_c Regions

The protein sequences of the C_H1 and F_c regions of the five human immunoglobulin classes (including γ subclasses γ_1 and γ_3) are presented in Fig. 4. The sequences have been aligned to display the homology of the sequences to one another. Positions that are invariant or highly conserved between the six sequences are indicated. The positions of the β strands are placed and numbered according to the scheme of Edmundson et al. (18). There are three amino acids that are invariant in all three domains: the two cysteines that form the intrachain disulfide bond and a tryptophan that is thought to protect the disulfide bond from reduction by solvent. It is clear that the most conserved amino acids between the classes lie in the β strands. This observation is repeated in the data presented in Fig. 5, where the four domains of the μ chain are aligned with the κ and λ constant regions. The overall homology between these domains is approximately 22%, with nearly all the homologous residues centered around the invariant cysteines and tryptophan and in the β strands. Note in Fig. 4 that the F_c sequences of μ and α have 18 extra amino acids at their carboxyl end. This extra segment is the site of J chain attachment involved in the formation of IgA and IgM multimers (21).

The overall identity of the F_c regions of the various classes is approximately 30%. The identity of γ and ε is significantly higher than this average. Different domains show different interclass homologies, the C_H1 domain being most similar at 33%, probably a reflection of the common function of pairing with immunoglobulin light chains. At an average identity of 41%, the carboxy terminal domains of μ, α, and γ are significantly more relat

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Date of Transmission: April 11, 2003

Attorney Docket No.23254-501

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS :	Holgersson et al.		
SERIAL NUMBER :	09/194,396	EXAMINER :	G. Ewoldt
FILING DATE :	December 8, 1998	ART UNIT :	1644
FOR :	ANTIGENIC FUSIONPROTEIN CARRYING GALα 1,3GAL EPITOPES		

BOX AF
Assistant Commissioner for Patents
Washington, D.C. 20231

PETITION FOR EXTENSION OF TIME

Pursuant to 37 C.F.R. §1.136(a), Applicants hereby petition for a two-month extension of time to respond to the November 12, 2002 Office Action in the above-identified application.

The Commissioner is authorized to charge the amount of $205.00 for the extension fee required under 37 C.F.R. §1.17(a)(2) and any additional fees that may be due, or to credit any overpayment, to the undersigned's account, Deposit Account No. 50-0311, Ref. No. 23254-501.

Respectfully submitted,

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Dated: April 11, 2003

By Facsimile: 703-872-9305
Date of Deposit: April 11, 2003

Attorney Docket No. 23254-501

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS:	Holgersson et al.		
SERIAL NUMBER:	09/194,396	EXAMINER:	G. Ewoldt
FILING DATE:	December 8, 1998	ART UNIT:	1644
FOR:	ANTIGENIC FUSION PROTEIN CARRYING GAL α1, 3 GAL EPITOPES		

BOX AF
Assistant Commissioner for Patents
Washington, D.C. 20231

NOTICE OF APPEAL

Pursuant to 37 C.F.R. §1.191, Applicants hereby appeal to the Board of Patent Appeals and Interferences from the Examiner's November 12, 2002 Office Action, finally rejecting the claims in the above-identified application. 37 C.F.R. § 1.17(b). Applicants have filed concurrently a petition for a two-month extension of time. With the extension, the Notice of Appeal is due on or before April 14, 2003, (April 12, 2003 being a Saturday).

The Commissioner is authorized to charge the amount of $160.00 for the Notice of Appeal and any additional fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Ref. No. 23254-501. A duplicate copy of this Notice is enclosed.

Respectfully submitted,

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Dated: April 11, 2003

J.AK

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/194,396	12/08/1998	JAN HOLGERSSON	45115-53906	3163

30623 7590 06/25/2003

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EXAMINER	
EWOLDT, GERALD R	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/25/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Notice of Abandonment

Application No.	Applicant(s)
09/194,396	Holgersson et al.
Examiner	**Art Unit**
G.R. Ewoldt, Ph.D.	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

This application is abandoned in view of:

1. ☒ Applicant's failure to timely file a proper reply to the Office letter mailed on *Nov 12, 2002* .

   (a) ☐ A reply was received on _____ (with a Certificate of Mailing or Transmission dated _____), which is after the expiration of the period for reply (including a total extension of time of ____ month(s)) which expired on _____ .

   (b) ☐ A proposed reply was received on _____ , but it does not constitute a proper reply under 37 CFR 1.113(a) to the final rejection.

   (A proper reply under 37 CFR 1.113 to a final rejection consists only of: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114).

   (c) ☐ A reply was received on _____ but it does not constitute a proper reply, or a bona fide attempt at a proper reply, to the non-final rejection. See 37 CFR 1.85(a) and 1.111. (See explanation in box 7 below).

   (d) ☒ No reply has been received.

2. ☐ Applicant's failure to timely pay the required issue fee and publication fee, if applicable, within the statutory period of three months from the mailing date of the Notice of Allowance (PTOL-85).

   (a) ☐ The issue fee and publication fee, if applicable, was received on _____ (with a Certificate of Mailing or Transmission dated _____), which is after the expiration of the statutory period for payment of the issue fee (and publication fee) set in the Notice of Allowance (PTOL-85).

   (b) ☐ The submitted issue fee of $_____ is insufficient. A balance of $_____ is due.

   The issue fee required by 37 CFR 1.18 is $_____ . The publication fee, if required by 37 CFR 1.18(d) is $_____

   (c) ☐ The issue fee and publication fee, if applicable, has not been received.

3. ☐ Applicant's failure to timely file corrected drawings as required by, and within the three-month period set in, the Notice of Allowability (PTO-37).

   (a) ☐ Proposed new formal drawings were received on _____ (with a Certificate of Mailing or Transmission dated _____), which is after the expiration of the period for reply.

   (b) ☐ No corrected drawings have been received.

4. ☐ The letter of express abandonment which is signed by the attorney or agent of record, the assignee of the entire interest, or all of the applicants.

5. ☐ The letter of express abandonment which is signed by an attorney or agent (acting in a representative capacity under 37 CFR 1.34(a)) upon the filing of a continuing application.

6. ☐ The decision by the Board of Patent Appeals and Interferences rendered on _____ and because the period for seeking court review of the decision has expired and there are no allowed claims.

7. ☐ The reason(s) below:

6/17/03

G.R. EWOLDT, PH.D.
PRIMARY EXAMINER
ART UNIT 1644

Petitions to revive under 37 CFR 1.137(a) or (b), or requests to withdraw the holding of abandonment under 37 CFR 1.181, should be promptly filed to minimize any negative effects on patent term.

VIA FACSIMILE
Date of Deposit: April 11, 2003

Attorney Docket No: 23254-501

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS: Holgersson et al.
SERIAL NUMBER: 09/194,396 EXAMINER Gerald Ewoldt
FILING DATE: December 8, 1998 ART UNIT: 1644
FOR: ANTIGENIC FUSIONPROTEIN CARRYING GALa 1,3 GAL EPITOPES

Commissioner for Patents
Washington, D.C. 20231

Certificate of Transmission under 37 CFR 1.8

I hereby certify that this correspondence is being facsimile transmitted to the United States Patent and Trademark Office on **April 11, 2003**.

Marie Sulkey
Signature

Marie Sulkey
Name of person signing the Certificate

The papers submitted with this facsimile include:

1. Amendment and Response to Office Action Mailed November 12, 2002 (8 pgs);
2. Copy of Hasemann and Capra, Fundamental Immunology, 2nd Edition (25 pgs);
3. Petition for a Two-Month Extension of Time (1 pg)
4. Notice of Appeal (1 pg); and,
5. Certificate of Transmission under 37 CFR 1.8 (1 pg.)

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DATE: April 11, 2003

FROM: Cynthia A. Kozakiewicz, Ph.D.

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ckozakiewicz@mintz.com

TO:

NAME	COMPANY	BUSINESS #	FAX #
Examiner Gerald Ewoldt	US Patent and Trademark Office		703 872-9305

MESSAGE:

Re: U.S.S.N. 09/194,396
Title: ANTIGENIC FUSIONPROTEIN CARRYING GALa 1,3 GAL EPITOPES
Filed: December 8, 1998
Attorney Docket No. 23254-501